Human developmental chondrogenesis as a basis for engineering chondrocytes from pluripotent stem cells.

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Authors: Ling Wu, Carolina Bluguermann, Levon Kyupelyan, Brooke Latour, Stephanie Gonzalez, Saumya Shah, Zoran Galic, Sundi Ge, Yuhua Zhu, Frank A Petrigliano, Ali Nsair, Santiago G Miriuka, Xinmin Li, Karen M Lyons, Gay M Crooks, David R McAllister, Ben Van Handel, John S Adams, Denis Evseenko

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Public Summary:
This paper describes fundamental features of human cartilage and joint development and defines critical differences and similarities between pluripotent stem cell derived cartilage and primary cartilage cells found at different stages of human development.

Scientific Abstract:
Joint injury and osteoarthritis affect millions of people worldwide, but attempts to generate articular cartilage using adult stem/progenitor cells have been unsuccessful. We hypothesized that recapitulation of the human developmental chondrogenic program using pluripotent stem cells (PSCs) may represent a superior approach for cartilage restoration. Using laser-capture microdissection followed by microarray analysis, we first defined a surface phenotype (CD166(low/neg)CD146(low/neg)CD73(+)CD44(low)BMPR1B(+)) distinguishing the earliest cartilage committed cells (prechondrocytes) at 5-6 weeks of development. Functional studies confirmed these cells are chondrocyte progenitors. From 12 weeks, only the superficial layers of articular cartilage were enriched in cells with this progenitor phenotype. Isolation of cells with a similar immunophenotype from differentiating human PSCs revealed a population of CD166(low/neg)BMPR1B(+) putative cartilage-committed progenitors. Taken as a whole, these data define a developmental approach for the generation of highly purified functional human chondrocytes from PSCs that could enable substantial progress in cartilage tissue engineering.